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10/574,016	03/29/2006	Yuji Ueno	Q107169	4347

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EXAMINER	
KIM, YUNSOO	
ART UNIT	PAPER NUMBER
1644	

NOTIFICATION DATE	DELIVERY MODE
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/574,016	UENO ET AL.	
	Examiner	Art Unit	
	YUNSOO KIM	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10 January 2010*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-11,14,15 and 18-21* is/are pending in the application.

4a) Of the above claim(s) *1-11* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *14,15,18-21* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Claims 1-11, 14, 15, and 18-21 are pending.

Claims 1-11 stand withdrawn from further consideration by the examiner under 37CFR 1.142(b) as being drawn to a nonelected invention.

Claims 14, 15, and 18-21 drawn to a solution-type antibody preparation are under consideration in the instant application.

2. The following rejections remain.

3. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office Action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

4. Claims 14, 15, and 18-20 stand rejected under 35 U.S.C. 103(a) as being unpatentable over EP 1174148A1 (IDS reference, of record) in view of U.S. 2003/019316A1, of record, for the reasons set forth in the office action mailed on 5/13/10.

The '148 publication teaches an antibody formulation comprising a humanized antibody, sodium citrate and a non-ionic surfactant (claims 1-8). The '148 publication further teaches the concentration of the antibody is 5-50 mg/ml ([0008]), pH of the preparation ranges 4.9-5.95 and the buffer concentration of 10mM (table 1, [0028-0029]).

As the specification of the instant application discloses (p. 17) the sodium citrate as a preferred example of citric acid, the referenced "sodium citrate" meets this limitation.

Further, the '148 publication teaches that the buffers may be used alone or as a combination of two or more and the exemplary buffers include phosphate, citrate, acetate, tartarate, malate, and arginine ([0014], claims 6-7) and a further addition of polysorbate (claim 8) in the presence of sodium citrate and/or phosphate.

The disclosure of the '148 publication differs form the instant claimed invention in that it does not teach the addition of glycine at the concentration of 10-30 mg/ml as is currently recited in claim 14 of the instant application.

The '316 publication teaches addition of glycine improves stabilization of preparation as it reduces aggregation ([0089]). The '316 publication teaches the glycine concentration of 200mM (example 4) which is equivalent to 15mg/ml as the molecular weight of glycine is 75g (see section 8 of the office action mailed 8/4/08). Therefore, it meets the limitation of claim 14.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to add glycine and/or substitute other buffers with glycine as taught by the '316 publication to the antibody formulation as taught by the '148 publication.

One of ordinary skill in the art at the time the invention was made would have been motivated to do so because the addition of glycine improves the stability of the antibody formulation by reducing aggregation. Therefore, it is prima facie obvious to combine two compositions each of which is taught by prior art to be useful for same purpose in order to form third composition that is to be used for very same purpose; idea of combining them flows logically from their having been individually taught in prior art. In re Kerkhoven, 205 USPQ 1069, CCPA 1980. See MPEP 2144.06

From the teachings of references, it would have been obvious to one of ordinary skill in art to combine the teachings of the references and there would have been a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was prima facie obvious to one of the ordinary in the art at the time of invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

Applicant's arguments filed on 11/10/10 have been fully considered but they were not persuasive.

Applicant has asserted that the Examiner's analysis of Table 1 of the '148 publication is flawed and one of ordinary skilled in the art would not select citrate over phosphate based on the Table 1 of the '148 publication. Applicant has further asserted the '148 publication teaches away from using citrate. Applicant has also stated that the combination of the citrate and phosphate buffer would not expect to improve stability at the higher temperature and one of skilled in the art would not have motivated to combine two buffers to yield the less stable composition (p. 5). Moreover, Applicant has asserted that the level of antibody aggregation is higher in citrate buffer than in phosphate and a skilled person would not combine these two buffers. Further, Applicant has provided the Hosokawa declaration (previously considered) to show unexpected results of the antibody composition comprising citric acid and glycine in soluble association and chemical degradation (p. 3-4 of the declaration).

Contrary to Applicant's assertion that the examiner's analysis of table 1 of the '148 publication is flawed, the '148 publication clearly indicates that the inventive and comparative formulations disclosed in table 1 are to compare stability [0028-29]). Unlike Applicant's assertion, the pharmaceutical compositions in inventive formulation are considered stable. The table 1 of the '148 publication can be analyzed horizontally comparing inventive and comparative or vertically comparing the temperatures at 40°C and 60°C. In addition, the claims of the '148 publication and the disclosure clearly states that the phosphate buffer and citrate buffer are combined (claim 6, p.3, lines 50-53).

Given that the prior art of record clearly suggests the combination of the phosphate and citrate buffer, it is Applicant's burden to demonstrate that such combination cannot be made. The previously considered Hosokawa declaration does not demonstrate that but the declaration is based on one buffer composition. Further, upon entry of the 1/20/10 amendment to the claims, the claimed invention no longer requires stabilization of the antibody by suppressing soluble association antibody. Note that the claimed antibody preparation reads on any preparation **comprising** an antibody, citrate and glycine at particular concentration. Given that the term comprising considered open ended, the claimed does not exclude addition of the phosphate. Further, note that the '148 publication is a primary reference and the '148 publication teaches the buffer is phosphate and/or citrate as recited in claim 6. As noted, the buffer system suggested by the '148 publication is citrate, phosphate, and citrate and phosphate. Therefore, Applicant's assertion based on that on of skilled in art would not combine phosphate and citrate is flawed.

As previously discussed, the '148 publication summarizes two sets of results, one set is at 40°C and the other is at 60°C or acidic and basic pH. From the table 1, it is evident that phosphate buffer showed a higher stability at 40°C but citrate buffer has shown higher resistance at the heat treatment at 60°C. Note that the phosphate buffer has shown no degradation (100 to 100) at 40°C but 19 % degradation at 60°C (100 to 81, table 1, lines 10-11) while citrate buffer has shown only 4% degradation at 60°C (81-77, table 1, lines 15-16).

Given that there is a need for developing stabilizing antibody formulation to cover broader temperature ranges during transport ([0002-0005]), the citrate buffer shown more resistant to degradation at higher temperature is a preferred buffer choice especially the '148 publication teaches the buffers of the invention may be used in combination of two or more (p.3, lines 54, [0014]). Therefore, the '148 publication does not teach away from combining phosphate buffer and citrate, the claimed invention of the instant application does not exclude phosphate. Note claim 14 of the instant application uses "comprises" and this term is considered open and allows adding other components. See MPEP 2111.

Further, claim 6 of the '148 publication recites acidic buffer to be sodium phosphate and/or sodium citrate. Therefore, Applicant's assertion that the '148 publication teaches away from combining citrate and phosphate is flawed. Note that the rejection is formulated to combine the '148 publication and the '316 publication. The motivation to add glycine is from the '316 publication as stated above.

Applicant has asserted that the Hosokawa Declaration (previously considered) shows the unexpected results and does not agree with Examiner's assessment of the declaration. Applicant has further asserted that the well settled law does not require demonstration of every unexpected result of claimed properties (p. 9-10 of response filed on 1/20/10).

Moreover, Applicant's reliance on unexpected results does not overcome clear and convincing evidence of obviousness. MPEP 2131.04. The declaration of Hosokawa (previously considered) states that the unexpectedly higher suppression of soluble association has been observed in the formulation comprising glycine and citric acid. Further, the declaration of Hosokawa (previously considered) is insufficient to overcome the rejection because it is not commensurate in scope of the claimed invention.

Note the currently claimed formulation is NOT required to exhibit suppression of chemical degradation.

As stated in the office action mailed 5/13/10, the declaration of Hosokawa fails to show unexpected results of showing chemical degradation of the composition comprising glycine and citric acid (see column 3, table 2). Further, the declaration of Hosokawa shows unexpected results of soluble association with the formulation C comprising KM-871 antibody at concentration of 2mg/ml, glycine at 23mg/ml and citrate acid at 10mM at pH 6.

However, the claimed composition is not limited to KM-871 antibody and the conditions stated in the declaration which exhibited unexpected results are not recited in the independent claim. Given that the independent claim does not recite a particular antibody (e.g. KM-871 antibody) and conditions (concentration and pH) which have shown unexpected results, the declaration is not sufficient to show the observation is truly unexpected. Therefore, the combination of references remains obvious.

Given that the asserted unexpected properties (e.g. suppress soluble association of the antibody, chemical degradation of antibody and insoluble aggregation of the antibody) are no longer required in the claimed preparation, the prior art references provides reasonable motivation to combine the references (e.g. addition of glycine reduces aggregation and thus improves overall stability of the antibody formulation).

As stated earlier, one of ordinary skill in the art at the time the invention was made would have been motivated to do so because the addition of glycine improves the stability of the antibody formulation by reducing aggregation. Therefore, it is prima facie obvious to combine two compositions each of which is taught by prior art to be useful for same purpose in order to form third composition that is to be used for very same purpose; idea of combining them flows logically from their having been individually taught in prior art. In re Kerkhoven, 205 USPQ 1069, CCPA 1980. See MPEP 2144.06.

Therefore, the combination of references remains obvious.

5. Claim 21 stands rejected under 35 U.S.C. 103(a) as being unpatentable over EP 1174148A1 (IDS reference, of record) in view of U.S. 2003/019316A1, of record, as applied to claims 14, 15 and 18-20 above further in view of U.S. Pat. No. 6,488,930B1, of record, for the reasons set forth in the office action mailed on 5/13/10.
The '148 publication and the '316 publication have been discussed, supra.

The disclosure of the '148 publication and the '316 publication differs form the instant claimed invention in that it does not teach a humanized antibody to CCR4 as is currently recited in claim 21 of the instant application.

The '930 patent teaches a composition comprising a humanized CCR4 antibody (claims 6 and 47).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to employ the stabilizing formation taught by the '148 publication and the '329 publication into a CCR4 humanized antibody taught by the '930 patent.

One of ordinary skill in the art at the time the invention was made would have been motivated to do so because the formulation taught by the '148 and the '329 publications improve stability of the antibody formulation.

From the teachings of references, it would have been obvious to one of ordinary skill in art to combine the teachings of the references and there would have been a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was prima facie obvious to one of the ordinary in the art at the time of invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

Applicant's arguments filed on 11/10/10 have been fully considered but they were not persuasive.

Applicant has asserted that the '148 publication teaches away from combining references because the level of antibody aggregation is higher in citrate buffer than in phosphate and a skilled person would not combine these two buffers. Further, Applicant has provided the Hosokawa declaration to show unexpected results of the antibody composition comprising citric acid and glycine in soluble association and chemical degradation.

In light of the discussion above in section 4 of this office action, the rejection remains obvious.

6. No claims are allowable.

7. THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

8. Any inquiry concerning this communication or earlier communications from the examiner should be directed to YUNSOO KIM whose telephone number is (571)272-3176. The examiner can normally be reached on M-F,9-5. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla can be reached on 571-272-0735. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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January 5, 2011

/Michael Szperka/
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